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Cardiac magnetic resonance imaging to detect ischemia in chronic coronary syndromes: state of the art

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KEY WORDS

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ABSTRACT

The new 2019 European Society of Cardiology guidelines for the diagnosis and management of chronic coronary syndromes emphasize the role of noninvasive functional imaging of myocardial ischemia in diagnosing coronary artery disease to guide decision making regarding revascularization. Cardiac magnetic resonance imaging (CMR) stands out relative to other imaging modalities given its high safety profile, absence of ionizing radiation, and its versatility in encoding various image contrasts. It also allows an assessment of myocardial function, ischemia, and viability as well as permits tissue characterization including detection of edema in a single examination. In recent years, a number of meta-analyses and studies considering the role of CMR for detecting ischemia have been published. The recent multicenter randomized MR-INFORM trial has demonstrated the clinical utility of CMR in patients with stable angina and cardiovascular risk factors. This landmark study has proved that a perfusion CMR-based strategy leads to a lower number of revascularizations while being noninferior to an invasive coronary angiography with fractional flow reserve-guided therapy in terms of major adverse cardiac events at 1 year. In light of recent and future technical improvements, CMR will become increasingly important in the assessment of myocardial ischemia in patients with chronic coronary syndromes.

Introduction Despite the tremendous improvement in diagnostic and therapeutic options during the last decades, ischemic heart disease remains the leading cause of death worldwide, accounting for about 17% of all deaths and 10% of years of life lost according to the recent World Health Organization report.¹ In Poland, ischemic heart disease is also accountable for the highest number of years of life lost by one person who died: each man who died from ischemic heart disease in 2014 lost on average 18 years of life, whereas each woman lost 11 years of life.² Ischemic heart disease is a chronic progressive disease caused by coronary atherosclerosis, functional alterations of epicardial vessels, and/or impairment of microcirculation. All these conditions can be present quiescently for many years

in a preclinical phase, before transforming into a stable symptomatic phase or an acute coronary syndrome, possibly leading to ischemic cardiomyopathy and heart failure.^{3,4}

Cardiac magnetic resonance imaging (CMR) is a noninvasive imaging modality with high reproducibility, safety, and cost-effectiveness.^{5,6} It is characterized by unparalleled versatility in terms of assessing cardiac function and morphology, for which CMR is the reference imaging method.⁷ CMR using late gadolinium enhancement (LGE-CMR) is the gold standard for detecting the presence and extent of infarct scar, being a strong predictor of clinical outcomes.^{3,8,9}

The aim of our review was to comprehensively summarize up-to-date knowledge of the diagnostic utility of CMR for detecting myocardial

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ischemia in chronic coronary syndromes (CCS) and for guiding revascularization.

The ischemic cascade Angina pectoris and myocardial infarction occur late in patients suffering from coronary artery disease (CAD), being the last stage in the ischemic cascade. The first steps may be asymptomatic; therefore, sensitive diagnostic tests are needed. At the very beginning of the ischemic cascade, an imbalance between oxygen supply and demand occurs, causing a reduction of myocardial perfusion, followed by left ventricular (LV) diastolic dysfunction and regional wall motion abnormalities. Later, electrical alteration develops that can be observed on electrocardiography (ECG). Finally, patients experience chest pain (FIGURE 1). The detection of myocardial perfusion defects is crucial for the early diagnosis of ischemia, because it appears earlier than diastolic and systolic dysfunction assessed by echocardiography or ECG. Evaluation and prompt management of silent myocardial ischemia could prevent angina pectoris and acute coronary syndrome in patients with CAD.^{7,10,11}

Role of noninvasive diagnostic techniques in patients with suspected coronary artery disease

The 2019 European Society of Cardiology (ESC) guidelines for the diagnosis and management of chronic coronary syndromes emphasize the importance of assessing the clinical likelihood of CAD to avoid unnecessary diagnostic tests and possible false-positive results. Noninvasive diagnostics is recommended for patients, with a pretest probability (PTP) of more than 15%. Due to a newly defined PTP threshold and in the light of current clinical practice, the guidelines also allow to consider diagnostic testing in patients with lower PTP (5%–15%). However, the higher likelihood of a false-positive result must be taken into account, and the individual decision should be made according to clinical judgment, patient

preference, and local resources. A presence of determinants of the clinical likelihood of CAD, including cardiovascular risk factors, changes in resting ECG, LV dysfunction, abnormal exercise ECG, and coronary calcium assessable by computed tomography (CT) should be evaluated for a more accurate estimation of individual PTP.

The new guidelines allow the use of either coronary CT angiography (CCTA) or noninvasive functional imaging of ischemia (by means of CMR, stress echocardiography, myocardial perfusion scintigraphy by single-photon emission CT [SPECT] or positron emission tomography) as the initial diagnostic test. However, in the case of coronary stenosis detected by CCTA or invasive angiography, further noninvasive or invasive functional testing is recommended for revascularization decisions (with exclusion of >90% diameter stenosis detected during invasive angiography). Therefore, CCTA should be used mainly in patients with low PTP, without previous diagnosis of CAD, and when good image quality is expected. In young patients, techniques without radiation (ie, CMR, stress echocardiography) are preferred.⁴

Ischemia detection in chronic coronary syndromes

According to the current 2018 ESC / European Association for Cardio-Thoracic Surgery guidelines on myocardial revascularization, noninvasive functional imaging is recommended as the first-line approach in patients with CCS, regional wall motion abnormalities, or reduced LV ejection fraction (LVEF), who are considered suitable for subsequent coronary revascularization.^{4,12}

Although conventional exercise stress test can reflect the real physical capacities of patients, it has numerous limitations. Due to low sensitivity and specificity in detecting obstructive CAD, it may be considered as an alternative diagnostic test only when other methods are unavailable.⁴ Superior diagnostic ability of stress imaging may distinguish patients who should

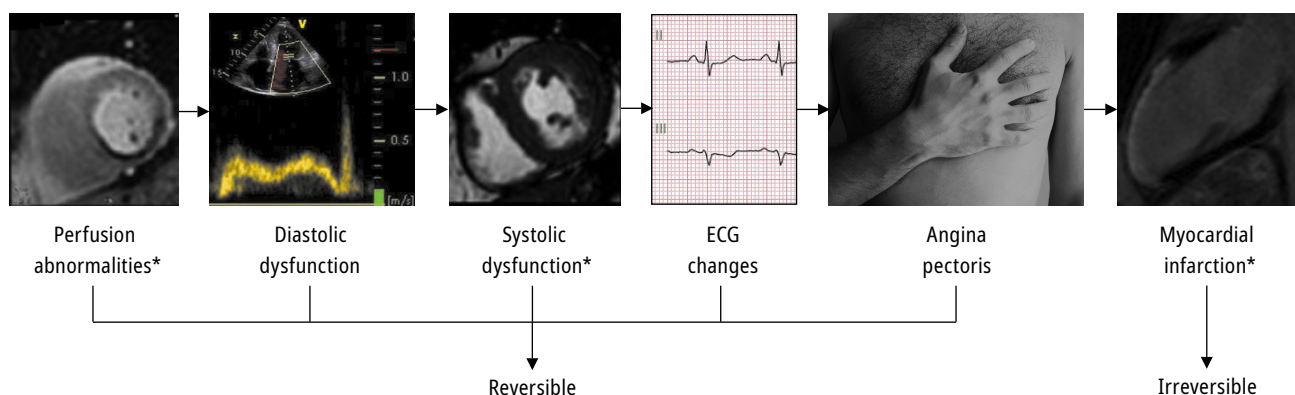


FIGURE 1 The ischemic cascade. Asterisks indicate the stages of ischemic cascade that are routinely assessed by cardiac magnetic resonance imaging.

Abbreviations: ECG, electrocardiographic

undergo revascularization to improve their prognosis from those who will not benefit from invasive management.^{4,12} The current ESC guidelines do not favor any of the stress imaging techniques, but simply describe advantages and disadvantages of each method.^{4,12}

Stress cardiac magnetic resonance imaging and evidence-based medicine

To confirm the role of CMR in the detection of cardiac ischemia, a few large randomized clinical trials have been conducted. To date, there have been 3 major clinical trials (MR-IMPACT [Magnetic Resonance Imaging for Myocardial Perfusion Assessment in Coronary Artery Disease Trial],¹³ MR-IMPACT II,^{14,15} and CE-MARC [Clinical Evaluation of Magnetic Resonance Imaging in Coronary Heart Disease])^{16,17} comparing stress perfusion CMR imaging with SPECT. All 3 studies have shown noninferiority or superiority of CMR in the detection of ischemia. However, coronary X-ray angiography with only quantitative assessment of coronary stenosis was used as the reference standard.¹³⁻¹⁷ In the multicenter prospective CE-MARC 2 trial,^{18,19} 1202 patients with suspected CAD (PTP, 10%–90%) were randomized to adenosine-stress CMR-, SPECT-, or National Institute for Health and Care Excellence guideline-based management. This study has shown that CMR and SPECT significantly reduced the rates of unnecessary invasive coronary angiography (defined by a normal invasive fractional flow reserve [FFR >0.8 within 12 months]).^{18,19} A detailed comparison of the most important prospective randomized clinical trials for perfusion CMR is presented in Supplementary material, *Table S1*.

In June 2019, the results from the landmark multicenter study MR-INFORM (MR Perfusion Imaging to Guide Management of Patients With Stable Coronary Artery Disease), comparing adenosine-stress CMR with FFR in patients with CAD, were published.²⁰ A total of 918 patients with stable typical angina symptoms and at least 2 cardiovascular risk factors or positive exercise treadmill test results were randomized to either a CMR- or invasive FFR-based strategy to guide coronary revascularization. Revascularization was performed when ischemia was observed for at least 6% of the myocardium or FFR was measured to be 0.8 or lower in the noninvasive and invasive group, respectively. The MR-INFORM trial proved that adenosine-stress CMR is noninferior to invasive FFR in guiding coronary revascularization in patients with CCS. There was no difference in primary outcome defined by major adverse cardiac events (including all-cause mortality, nonfatal myocardial infarction, and target-vessel revascularization) between groups during the 12-month follow-up. In the CMR group, only 48% of patients underwent coronary angiography and 36% of patients

underwent index revascularization, whereas in the FFR group, 45% of patients underwent index revascularization. Therefore, the use of perfusion CMR was associated with a significantly lower number of invasive procedures.^{20,21}

In the literature, there are also numerous meta-analyses of stress perfusion CMR in comparison with other cardiac imaging methods and invasive FFR, which have confirmed the high diagnostic accuracy of CMR on both a per-patient and per-vessel basis.²²⁻²⁶ According to these meta-analyses, perfusion CMR has a sensitivity of 89% to 90% and specificity of 85% to 94% on a per-patient basis, as well as a sensitivity of 87% to 91% and specificity of 85% to 91% on a per-vessel basis, when compared with the gold standard of invasive FFR measurements.^{22,25,26}

Prognostic value of stress cardiac magnetic resonance imaging

The importance of stress perfusion CMR is not only due to its high diagnostic accuracy but also due to its ability to predict cardiac outcome and individual patient prognosis.^{6,27-34} Jahnke et al²⁸ have shown that pathological adenosine-stress CMR (defined as ≥ 1 segment with an inducible perfusion deficit of >25% transmural) or pathological dobutamine-stress CMR (≥ 1 segment with an inducible wall motion abnormality) identified patients at high risk for subsequent cardiac death or nonfatal myocardial infarction, whereas patients with normal stress CMR were at very low risk for cardiovascular events (3-year event-free survival, 84% vs 99%). Vincenti et al³¹ found that ischemia of at least 1.5 myocardial segments (equivalent to ~9% of the LV myocardium) in stress CMR was the strongest predictor of cardiac death, nonfatal acute myocardial infarction, and late coronary revascularization (>90 days after CMR). Patients without or with only one ischemic segment had excellent outcomes and could thus be spared revascularization.

A meta-analysis of 19 studies (14 with vasodilator stress, 4 with dobutamine, and 1 using both), including 11 636 patients with a mean follow-up of 32 months, highlighted that a negative stress CMR is associated with very low risk of cardiovascular death and acute myocardial infarction and therefore has an excellent prognostic value in patients with known or suspected CAD. No significant difference between vasodilator and dobutamine-stress CMR was observed.³⁰

Revascularization in chronic coronary syndromes

According to current ESC guidelines, myocardial revascularization is recommended for patients with CCS when symptoms of angina persist despite optimal medical therapy, including antianginal drugs. It should also be considered in patients with CAD and a large area of ischemia documented in a functional noninvasive

test (ie, >10% of the LV myocardium), abnormal invasive FFR, coronary stenosis exceeding 90%, or LVEF of 35% or lower due to CAD (Supplementary material, *Figure S1*).^{4,12} However, despite these recommendations, there is currently no conclusive evidence supporting prognostic benefits from routine revascularization in patients with CCS, significant myocardial ischemia, or hemodynamically relevant coronary artery stenosis; therefore, the best management is a subject of ongoing debate.^{4,12,35} For that reason, results from the ISCHEMIA trial (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches), which investigates whether coronary revascularization, in addition to optimal medical therapy, improves prognosis in patients with CCS and moderate-to-severe myocardial ischemia assessed by noninvasive imaging, are highly anticipated in early 2020.³⁶⁻³⁸

Stress cardiac magnetic resonance imaging for the assessment of myocardial ischemia Patients referred for CMR for assessing the presence and extent of ischemia undergo either perfusion CMR with a vasodilator (ie, adenosine, regadenoson, or dipyridamole) and gadolinium contrast media (CM) or dobutamine-stress CMR with wall motion analysis. Administration of CM gives the unique opportunity to combine the diagnosis of myocardial ischemia with the determination of myocardial viability (LGE-CMR). Therefore, this comprehensive technique is preferred in daily clinical practice. However, in the case of contraindications to gadolinium-based CM, dobutamine-stress with assessment of inducible regional wall motion abnormalities is recommended. A comprehensive comparison of medications (adenosine, regadenoson, dipyridamole, and dobutamine) available for stress CMR is presented in *TABLE 1*.³⁹⁻⁵¹

Vasodilator stress perfusion cardiac magnetic resonance imaging During perfusion CMR, the first-pass transit of a gadolinium-based CM through the LV myocardium is observed under hyperemia mediated by infusion of a vasodilator. In the healthy myocardium, the coronary microvasculature dilates during exercise and stress ensuring suitable tissue perfusion, whereas for significantly stenosed coronary arteries, the distal microvasculature is almost maximally dilated under rest conditions and hyperemia provoked by vasodilators triggers a coronary steal effect. A CM used in CMR is a T₁-shortening agent; therefore, the rapid passage of the CM bolus through the normally perfused LV myocardium appears bright in T₁-sensitive pulse sequences, whereas hypoperfused segments remain darker. Usually, 3 short-axis slices are acquired every heartbeat, and the whole first-pass perfusion scan is performed during one breath-hold (*FIGURE 2*).^{7,40,49,52,53}

To date, the most common method to assess perfusion deficits is the visual evaluation performed by an experienced physician. However, semi-quantitative and quantitative methods may help objectify the study results in the near future. Semiquantitative analysis uses signal intensity changes over time during first-pass perfusion for each myocardial segment, whereas fully quantitative analysis is based on the calculation of the total myocardial blood flow using pharmacophysiological modelling.⁵⁴⁻⁵⁹

The great majority of clinical trials, including the recent MR-INFORM study, were performed on 1.5-T scanners (Supplementary material, *Table S1*), although 3.0-T scanners may potentially offer advantages with regard to temporal and spatial resolution and resulting diagnostic accuracy. The key problems of higher field strength are susceptibility artefacts, greater field inhomogeneity, and higher local energy deposition, which might be a limitation for numerous magnetic resonance imaging-conditional implants and devices.^{40,53,60-62}

Dobutamine-stress cardiac magnetic resonance imaging In contrast to first-pass perfusion imaging, where only differences in myocardial perfusion between the healthy and hypoperfused myocardium are visualized, dobutamine is an inotropic and chronotropic agent, which induces maximal vasodilation and therefore leads to true ischemia and LV wall motion abnormalities in patients with significant CAD. The protocol is similar to the one used in stress echocardiography with increasing doses of dobutamine and optional addition of atropine until the target heart rate is reached: 85% of the maximal predicted heart rate = $[(220 - \text{age}) \times 0.85 \text{ bpm}]$. During each stage lasting approximately 3 minutes, cine images are acquired in all 4 standard geometries (short-axis, 2-chamber, 3-chamber, and 4-chamber view; Supplementary material, *Figure S2*).

Inotropic stress is an alternative to vasodilator stress perfusion CMR in patients with severely impaired renal function or other contraindications to vasodilator medication or gadolinium-based CM.^{7,49,53,63,64} If there are no contraindications to the use of CM, dobutamine-stress CMR can be combined with first-pass perfusion to increase sensitivity.^{65,66}

In general, a sensitivity of 83% and a specificity of 86% on a per-patient level for the detection of CAD defined by quantitative angiography ($\geq 50\%$ diameter stenosis) was reported.⁶⁷

Assessment of infarct scar and viability of the myocardium The presence and severity of perfusion deficits should always be interpreted along with the presence and transmural extent of infarct scars, because revascularization should be limited to those cases where the ischemic myocardium has a potential to recover.

As the gadolinium-based CM is not able to enter the intracellular space, it is distributed in the extracellular volume in the healthy myocardium but also in myocytes with ruptured cell membrane. Therefore, late gadolinium enhancement (LGE) is visible on T₁-weighted CMR images as hyperenhancement in the necrotic myocardium. The subendocardial pattern of LGE allows to distinguish infarct scar from other myocardial fibrosis of nonischemic origin.^{7,49,53,68} The transmural of the infarct scar correlates

inversely with the viability of the myocardium (FIGURE 3).⁶⁹⁻⁷¹ It has been shown that infarct scars not exceeding 25% of the myocardial wall width are most likely to achieve functional recovery after revascularization, whereas segments with subendocardial hyperenhancement greater than 75% are unlikely to recover.⁷⁰ A 50% transmural of LGE has been proposed as the cutoff value to determine the viable myocardium that could potentially benefit from revascularization.⁷¹

TABLE 1 Comparison of cardiac magnetic resonance stress tests by pharmacological agents used (continued on the next page)

Criteria	Adenosine	Regadenoson	Dipyridamole	Dobutamine (+/- atropine)
Mechanism of action	Perfusion CMR with a vasodilator induces flow heterogeneity between normal and ischemic myocardium Nonselective adenosine receptor agonist	Selective low-affinity A _{2A} specific adenosine receptor agonist (very weak agonist of the A ₁ adenosine receptor, negligible affinity to A _{2B} and A ₃ adenosine receptors)	Indirect drug acts by blocking the cellular uptake and metabolism of endogenous adenosine.	Wall motion abnormality induced by ischemia β-adrenergic agonist with inotropic and chronotropic effect (primarily β ₁ -adrenergic catecholamine with mild α ₁ - and β ₂ -receptor agonist activity)
Patient preparation	Withhold coffee, tea, chocolate, and aminophylline/theophylline for 12–24 hours prior to CMR.			Withhold β-blockers, negatively chronotropic calcium antagonists, and nitrates for at least 24–48 hours prior to CMR (in order to achieve the target HR).
Contraindications	General	Severe claustrophobia (persistent after use of sedatives such as midazolam intranasal) MRI-unsafe metallic implants, devices, defibrillators or permanent pacemakers (recommended source: www.mrisafety.com)		
	Specific	Uncontrolled asthma (active ongoing wheezing) 2nd- or 3rd-degree AV block, type II 2nd-degree AV block, sick sinus syndrome Severe hypotension (SBP <90 mm Hg) ACS <24 hours Decompensated heart failure	Asthma or tendency to bronchospasm 2nd- or 3rd-degree AV block, type II 2nd-degree AV block, sick sinus syndrome Severe hypotension (SBP <90 mm Hg) ACS <4 weeks Recent unexplained syncope (within 4 weeks) or with recent TIA Left ventricular outflow obstruction or hemodynamic instability Myasthenia gravis	Uncontrolled arterial hypertension (≥220/120 mm Hg) ACS <3 days Severe aortic stenosis Myo-, endo-, pericarditis Uncontrolled cardiac decompensation Poorly controlled arrhythmias Hypertrophic obstructive cardiomyopathy Mobile thrombus in the left ventricle/ left atrium/ left atrial appendage Atropine: narrow angle glaucoma, advanced prostate hypertrophy, myasthenia gravis, obstructive uropathy, obstructive gastrointestinal disorders
Half-time	Approx. 5–10 s (onset of action after 30 s)	Approx. 2–5 min (initial phase: 2–4 min; intermediate phase: 30 min, this phase coincides with a loss of the pharmacodynamic effect; terminal phase: 2 hours)	Approx. 30 min	Approx. 2 min
Administration	2 IV cannulas (for separate administration of CM and vasodilator)	1 IV cannulas	2 IV cannulas (for separate administration of CM and vasodilator)	1 or 2 IV cannulas (1 if study without CM)

TABLE 1 Comparison of cardiac magnetic resonance stress tests by pharmacological agents used (continued from the previous page)

Criteria	Adenosine	Regadenoson	Dipyridamole	Dobutamine (+/- atropine)
CMR protocol	ECG and BP monitoring system, CMR conditional monitoring system, defibrillator, resuscitation material, CMR conditional drug infusion pumps or placed outside of the room with long lines to feed into the scanner room			
Equipment				
Agent dosage	Adenosine infusion at 140 µg/min/kg for at least 3 min (when no response observed increase dose to 170 µg/min/kg; if still not sufficient, 210 µg/min/kg)	Regadenoson infusion bolus (0.4 mg in a rapid IV injection for approx. 10 s)	Dipyridamole infusion dose of 0.56 mg/kg for 4 min If needed: 2nd dose of 0.28 mg/kg for 2 min or 0.86 mg/kg for 6 min	Dobutamine infusion at different doses in several stages: 10, 20, 30, 40 µg/kg/min at 3–5 min per stage until 85% of the maximal predicted HR ($0.85 \times [220 - \text{age}]$) is reached. If the target HR is not achieved, doses of atropine may be added (0.5–2 mg IV).
Imaging	Bolus injection of gadolinium CM (0.05–0.1 mmol/kg) and first-pass perfusion imaging (3 short-axis slices by every heartbeat) Rest perfusion imaging after injection of a 2nd contrast dose (this study can be omitted in case of severe kidney disease), followed by LGE imaging			During each stage: cine images in 3 long-axis views and min. 3 short-axis slices are acquired.
Evaluation of positive response	Hemodynamic response (increase of heart rate >10 bpm or drop of SBP >10 mm Hg) Symptoms (heat, difficulty breathing, tolerable chest pain, facial flushing) Splenic switch off (only for adenosine)			Target HR
Side effects and complications	Flushing (35%–40%), chest pain (25%–30%), dyspnea (20%), dizziness (7%), nausea (5%) Symptomatic hypotension (5%) AV block (8%), 2nd-degree AV block (4%), complete heart block (<1%); Bronchospasm (0.1%) AMI (extremely rare)	Dyspnea (29%), headache (27%), flushing (23%), chest pain (19%), gastrointestinal discomfort (15%), dizziness (11%) Rhythm or conduction abnormalities (26%), 1st-degree AV block (3%), 2nd-degree AV block (0.1%), ventricular conduction abnormalities (6%) Paresthesia, hypoesthesia, dysgeusia (0.01–0.1%) Throat tightness, throat irritation, cough (0.01%–0.1%) AMI (extremely rare) Adverse reactions usually resolve during 15–30 min	Headache, dizziness (>0.1%) Chest pain (>0.1%) Hypotension (0.01%–0.1%) Paresthesia, flushing, nausea (0.01%–0.1%) UA (0.02%) Acute pulmonary edema (0.02%) VT (0.01%) AF (0.01%) Asystole (0.01%) TIA (0.01%) AMI (extremely rare)	Severe chest pain (1%) Severe dyspnea (1%) Nausea (0.4%) Urinary urgency (0.1%) Hypertension $\geq 220/120$ mm Hg (0.5%) Decrease in SBP >40 mm Hg (0.3%) VT (1.24%) AF (0.5%) AMI (0.09%) Rupture of the free wall of the left ventricle or septal defect (extremely rare)
Indications to stop examination	Hemodynamic and subjective positive response Frequent / complex cardiac arrhythmias Greater than transient AV block or severe bradycardia Decrease in SBP >40 mm Hg or severe hypotension (SBP <80 mm Hg) Wheezing Severe chest pain Patient request			Target HR achieved Severe angina pectoris or dyspnea Complex cardiac arrhythmias Decrease in SBP ≥ 40 mm Hg with change in reported symptoms Hypertension $\geq 240/120$ mm Hg New or worsening wall motion abnormalities in ≥ 1 segment Patient request
Antidote	Stop IV infusion Aminophylline / theophylline	Aminophylline / theophylline	Stop IV infusion Aminophylline / theophylline	Stop IV infusion Esmolol (β -blocker)

Abbreviations: ACS, acute coronary syndrome; AF, atrial fibrillation; AFI, atrial flutter; AMI, acute myocardial infarction; approx., approximately; AV, atrioventricular; BP, blood pressure; CM, contrast media; CMR, cardiac magnetic resonance imaging; COPD, chronic obstructive pulmonary disease; HR, heart rate; IV, intravenous; LGE, late gadolinium enhancement; MRI, magnetic resonance imaging; SBP, systolic blood pressure; TIA, transient ischemic attack; UA, unstable angina; VT, ventricular tachycardia; others, see [FIGURE 1](#)

It has been shown that infarct size and its transmural extent assessed by LGE-CMR are better predictors of mortality and significant cardiac events than LVEF and LV volume.^{72–75} Furthermore, patients with infarct scar present within the viable myocardium, who do

not undergo revascularization, have poorer survival.⁷³ It must be noted that the presence of infarct scar also predicts cardiovascular events in patients without a previous diagnosis of CAD and without LV regional wall motion abnormalities.^{72,76}

Standard CMR protocols for pharmacological stress and viability assessment are shown in Supplementary material, *Table S2*.

Future perspectives New techniques in CMR image reconstruction and automated quantitative analysis are developing rapidly and may become an alternative to a purely visual interpretation.^{56,58,77} Therefore, we would like to describe some innovative approaches that in our opinion have the potential to become an important part of standard CMR evaluation of ischemia in the next decade.

For precise differentiation of stress-induced myocardial ischemia and infarct scar, 3-dimensional (3D) image fusion of whole-heart dynamic CMR perfusion and LGE was proposed.⁷⁸ Whole-heart dynamic CMR perfusion is based on a new 3D acquisition sequences that allow readout of the entire examination volume at once in contrast to routinely used 2D acquisition of separate slices.⁷⁸⁻⁸⁴

Hybrid imaging holds promise for the field of cardiac imaging and planning of myocardial revascularization. It may be of particular value in multivessel disease, where the simultaneous

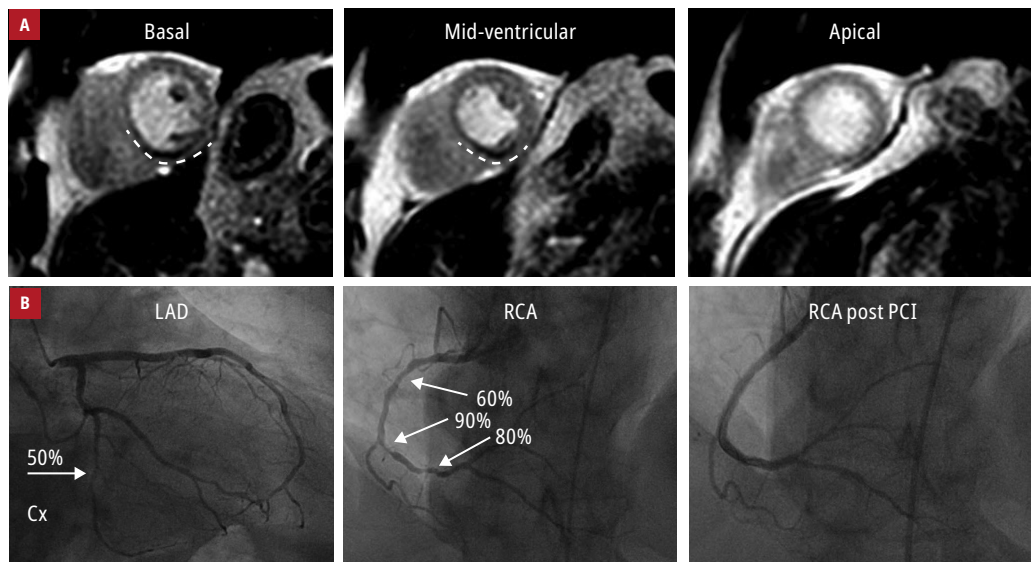


FIGURE 2 A 66-year-old physically active male patient with atypical chest pain (pretest probability, 26%) with cardiovascular risk factors (arterial hypertension, dyslipidemia, type 2 diabetes mellitus, adiposity, former smoking) was referred for stress cardiac magnetic resonance imaging (CMR). **A** – the 3 slices of a standard CMR perfusion with adenosin. Stress-induced ischemia is seen in 4 segments (inferoseptal and inferior basal to mid-ventricular [dashed lines]). No myocardial hypoperfusion was observed during perfusion CMR at rest. In CMR with late gadolinium enhancement, no infarct scar and nonischemic pattern of myocardial fibrosis were detected. **B** – the patient was referred for coronary angiography, which revealed 50% stenosis in the distal circumflex artery (Cx; small vessel) and serial high-grade stenosis (60%–90%) in the right coronary artery, which was successfully treated with 2 drug-eluting stents.

Abbreviations: LAD, left anterior descending coronary artery; PCI, percutaneous coronary intervention; RCA, right coronary artery

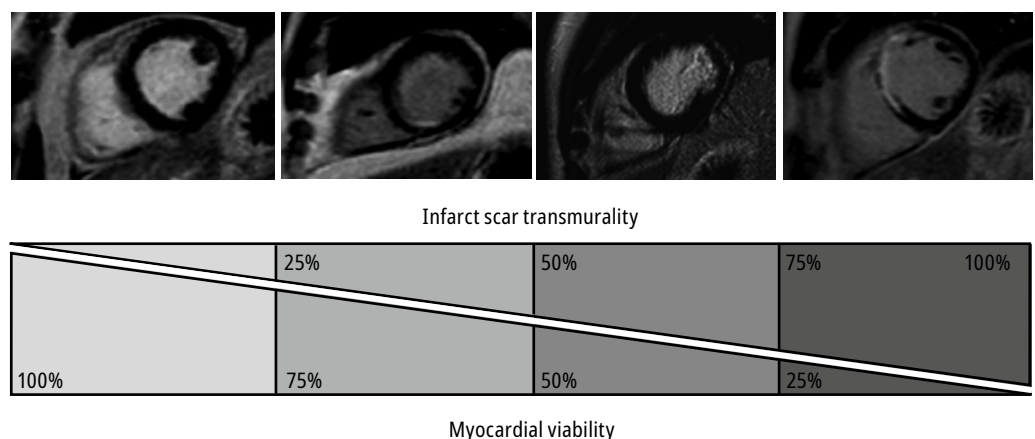


FIGURE 3 Graphical presentation of the association between myocardial viability and infarct scar transmural (cardiac magnetic resonance imaging with late gadolinium enhancement, short-axis view)

visualization of coronary stenosis and resulting stress perfusion deficits can help identify culprit lesions. In recent years, there has been a considerable interest in the combination of SPECT and CCTA, but this combination of modalities has the disadvantages of higher levels of ionizing radiation and suboptimal sensitivity of SPECT to detect CAD in comparison with stress perfusion CMR.^{13,85,86}

Therefore, a more promising option may be 3D fusion of CCTA and whole-heart dynamic 3D-CMR perfusion.⁸⁷ The method was recently extended to also include information on CT-derived FFR and myocardial scar (FIGURE 4). A possible future solution avoiding ionizing radiation is 3D fusion imaging of 3D-CMR perfusion data with 3D-CMR coronary angiography performed within a single CMR examination.⁸⁸

For patients with contraindications to vasodilator medication or gadolinium-based CM, it is important to provide alternative imaging tests for ischemia detection. One of the most promising CMR methods is T1 mapping performed during vasodilator stress, which has shown to distinguish obstructive epicardial CAD from microvascular dysfunction.⁸⁹ The technique, however, requires carefully designed imaging and processing protocols as effect sizes are relatively

small. Changes in T1 can be related to the fact that the microcirculatory arteries in the ischemic myocardium already dilate at rest and are not able to further respond to stress conditions. Therefore, due to the increased volume of myocardial blood, the T1 relaxation time is already prolonged at rest and does not change under stress conditions.⁸⁹⁻⁹¹

Another innovative noncontrast approach is the CMR blood oxygen level-dependent method, which uses the paramagnetic features of deoxyhemoglobin. An increased amount of this endogenous contrast agent results in signal reduction on T2*-weighted images and therefore indicates the myocardial oxygenation status during rest and vasodilator stress.⁹²⁻⁹⁴ A preliminary study showed that texture analysis of native CMR images may provide an alternative to CM-dependent LGE-CMR in the diagnosis of subacute and chronic infarction.⁹⁵ Finally, cardiac diffusion CMR allows an assessment of changes in myocardial extracellular volume and microstructure without the need for CM.⁹⁶⁻⁹⁸

Another developing technique is hyperpolarized carbon-13 CMR, capable of visualizing the uptake of metabolic substrates and their

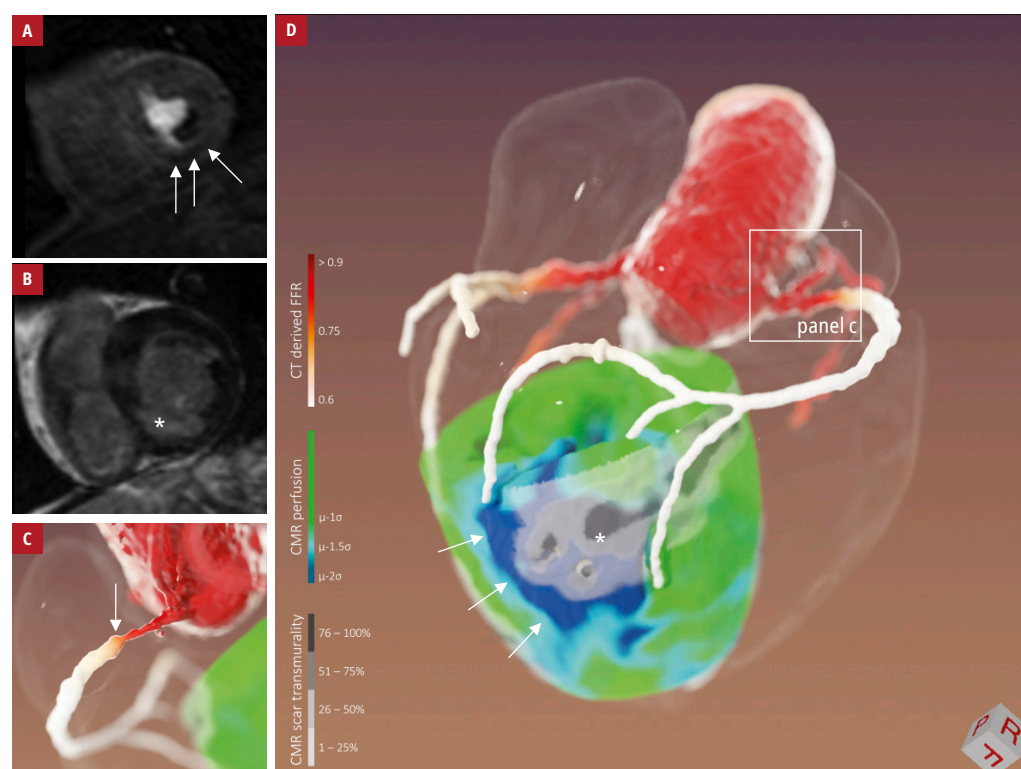


FIGURE 4 Three-dimensional (3D) image fusion combining information from coronary computed tomography angiography (CCTA), computed tomography (CT)-derived fractional flow reserve (FFR), stress perfusion cardiac magnetic resonance imaging (CMR), and CMR with late gadolinium enhancement (LGE-CMR). Data from a 59-year-old male patient with severe 3-vessel coronary artery disease are shown. Conventional 2-dimensional images of CT and CMR datasets (**A** – stress perfusion CMR; **B** – LGE-CMR) were postprocessed, coregistered, color-coded, and rendered in a 3D fashion. In CCTA, a subtotal proximal stenosis of the right coronary artery was found (**C** – 3D rendering, also note the associated drop of CT-derived FFR value), which resulted in an inferior/inferolateral perfusion deficit (arrowheads in **A** and **D**) as well as severe, partly transmural scar (asterisk in **B** and **D**).

intracellular transformation into downstream products. This metabolic CMR may potentially be involved also in evaluation of myocardial viability and ischemia in the future.^{99,100}

Conclusions As laid out in our review of the current literature, CMR plays a leading role in the diagnostic workup of patients with CCS. It allows an assessment of myocardial function, ischemia, and viability within a single noninvasive examination over a short period of time. Recent and future technical improvements will further increase its importance in the diagnostic assessment of myocardial ischemia and identification of patients who will most likely benefit from revascularization.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/kardiologiapolska.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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